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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/721,447	09/27/96	PINSKY	D 51917/JPW/JM

HM12/1021

JOHN P WHITE
COOPER AND DUNHAM
1185 AVENUE OF THE AMERICAS
NEW YORK NY 10036

EXAMINER	
DECLOUX, A	
ART UNIT	**PAPER NUMBER**
1644	19

DATE MAILED: 10/21/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/721,447	Pinsky et al
Examiner	**Group Art Unit**
Amy DeCloux	1644

☒ Responsive to communication(s) filed on *Aug 12, 1999* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *46-55* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *46-55* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The request filed 8/12/99 (Paper No. 17) for a continued Prosecution Application (CPA) under 37 CFR 1.53.(d) based on parent application No. 08/721447 is acceptable and a CPA has been established. An action on the CPA follows.

2. Applicant's amendment, filed 8/12/99 (Paper No. 18), is acknowledged.
Claims 29-38 have been canceled. Claims 1-28 and 39-45 have been canceled previously.
Claims 46-55 have been added and are being acted upon presently.

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are now currently directed and make some reference to Factor IXa. Applicant should restrict the title to the claimed invention.

4. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84. Please see form PTO-948 attached to a previous Office Action, mailed 10/28/97 (Paper No. 7). Applicant is reminded to change the Brief Description of the Drawings in accordance with any changes.

5. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected. "BALB/c" is the proper designation of this mouse strain, see page 77 of the specification, for example.

6. Claims 44-56 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed: "chemically inactivated Factor IXa".

Applicant's amendment, filed 8/12/99 (Paper No. 18), asserts that no new matter has been added. Applicant directs support to pages 17 and 110-112 for the written description for the above-mentioned chemically inactivated Factor IXa , and states that the newly added claims 46-55 correspond to original claims 29-38. However neither the specification nor the claims as originally filed provide a written description or set forth the metes and bounds of the above-mentioned chemically inactivated Factor IXa.

The specification does not provide blazemarks nor direction for the instant methods encompassing the above-mentioned chemically inactivated Factor IXa as they are currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action. Alternatively, applicant is invited to provide sufficient written support for the chemically inactivated Factor IXa indicated above or rely upon the limitations set forth in the specification as filed.

7. Claims 46-55 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

A) "Chemically" inactivated Factor IXa; Claims 46-55 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for a method which comprises administering any chemically inactivated Factor IXa to inhibit coagulation, as encompassed by claims 46-55. The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims. Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies any chemically inactivated Factor IXa, other than the heat inactivated Factor IX, as disclosed on page 17 of the specification. It is not clear that heat inactivation even encompasses chemical inactivation.

Furthermore, there is insufficient direction or guidance provided to assist one skilled in the art in the selection of any chemically inactivated Factor IXa, nor is there sufficient evidence provided that all such chemically inactivated Factor IXas could be used in a practical manner in a method to inhibit coagulation so as to thereby treat the ischemic disorder in the subject. It would require undue experimentation to produce all such possible chemically inactivated Factor IXas without more explicit guidance from the disclosure. It would require undue experimentation to investigate all such chemically inactivated Factor IXas with respect to their ability to inhibit coagulation.

B) Modes of Administration; Nor does there appear to be sufficient evidence that applicant's reliance on a method of intravenous administration of any inactivated Factor IXa to mice in a mouse model of cerebral ischemia disclosed in Example 9, would indicate that the claimed therapeutic modalities based upon the method which comprises administration of a pharmaceutically acceptable form of any inactivated Factor IXa wherein the carrier comprises an aerosol, oral or topical carrier, as encompassed by claim 50, would be effective to inhibit coagulation, commensurate in scope with the claimed invention. Additionally, applicant has not provided sufficient guidance and direction nor objective evidence that the skilled artisan can deliver a sufficient amount of chemically inactivated Factor IXa in an aerosol, oral or topical carrier as encompassed by claim 50, in treating an ischemic disorder. Ischemia comprises treating vascular disorders and it would not be predictable that one could deliver a therapeutic effect amount in such disorders other than intravascular routes of administration. In the absence of objective evidence to the contrary; aerosol, oral and topical carriers and means of delivery are not enabled for treating ischemia.

In view of the lack of predictability of the art to which the invention pertains, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for methods which comprise administering inactivated Factor IXa to inhibit coagulation so as to thereby treat the ischemic disorder in the subject.

8. Claims 46-55 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 46-55 are indefinite in the recitation of "chemically inactivated Factor IXa" because its characteristics are not known. It is not clear what type of chemical modifications are indicated and whether such chemical modifications include and/or are limited to those that are a result of heat as indicated on page 17 of the instant specification. Please clarify.

B) The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent

in the United States.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

12. Claim 46 and 47, 49-51 and 53-55 are rejected under 35 U.S.C. § 102(b) as being anticipated by Tijburg at al., (J. Biol. Chem. 266:12067-12074, 1991).

Tijburg et al teaches that infusion of chemically inactivated factor IXa prevented thrombus formation in the tumor vasculature of mice (see entire article especially 12072, column 1, lines 1-10, and page 12068, column 1, lines 6-21 of Section entitled "Preparation of Coagulation Proteins"). The definition of "ischemic disorders" disclosed on page 16 of the instant specification "encompasses and is not limited to a peripheral vascular disorder... or a stroke disorder". Therefore, the instant claims read on the method used in the tumor vasculature of mice, as taught by Tijburg. Tijburg also teaches an intravenous dosage of a total of 10 ug of chemically inactivated Factor IXa (see entire article, in particular page 12068, last paragraph of column 1, lines 9-12); assuming a mouse weighs 25 grams, then the dosage of chemically inactivated factor IXa taught is 400 ug/kg. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods.

13. Claims 46-55 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Tijburg at al., (J. Biol. Chem. 266:12067-12074, 1991) in view of Moller et al. (CA 2,141,642) see 1449.

Claims 46-55 are drawn to a method for treating an ischemic disorder comprising administering chemically inactivated Factor IXa to inhibit coagulation so as to thereby treat the ischemic disorder.

Tijburg et al teaches as described above. However, Tijburg et al do not apply their teachings to the breadth of ischemic events encompassed by the instant claims.

Moller teaches that proteolytic fragments of Factor IXa are able to inhibit the Factor IXa induced decrease of the thrombocyte count in vivo and teach their use in prophylaxis and therapy of thrombotic diseases (see entire article, in particular pages 1 lines 1-2. Page 3 line 25, Page 4 lines 1 & 2, Page 5 lines 10-17).

One of ordinary skill in the art at the time the invention was made would have been motivated to administer a chemically inactivated factor IXa as taught by Tijburg for use in tumors, in place of the proteolytic fragments of Factor IXa, as taught by Moller, in a method to treat thrombosis as taught by Moller, since both the chemically inactivated factor IXa and the proteolytic fragments of Factor IXa appear to exhibit the same or nearly the same structural and functional properties of inhibiting the activity of endogenous Factor IXa. The dosages and routes of administration (intravascular) were all known at the time the invention was made and would have depended upon the needs of the subject for a particular ischemia disorder.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Omum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 46-55 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of copending Application No. 09/053871. Although the conflicting claims are not identical, they are not patentably distinct from each other because they both encompass methods of inhibiting coagulation with an inactivated Factor IXa which appear to overlap one another. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 46-55 are directed to an invention not patentably distinct from claims 29-30 of commonly assigned copending application 09/053871. Specifically, the conflicting claims are patentably distinct from each other because both applications are drawn to the same or nearly the same methods of inhibiting coagulation with inactivated Factor IXa; the former application using chemically inactivated Factor IXa, the latter using inactive recombinant muteins of Factor IXa.

Commonly assigned copending application 09/053871, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. § 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. § 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 C.F.R. § 1.78© and U.S.C 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. § 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. § 102(f) or (g).

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy DeCloux whose telephone number is (703) 306-5821. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Amy DeCloux, Ph.D.
Patent Examiner, Group 1640, Technology Center 1600
October 20, 1999

PHILIP GAMBEL
PATENT EXAMINER
GROUP 1600

TECH CENTER 1600
10/20/99
PHILIP GAMBEL